

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Sohocki, M., et.al.

SERIAL NO.: 09/765,061

FILED: 01/17/01

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ART UNIT NO.:1645

EXAMINER: FRIEND, THF

DOCKET NO.:25630/16UTL

TITLE: Mutations in a Novel

Photoreceptor-Pineal Gene on 17p

Cause Leber Congenital Amaurosi (LCA4)

RECEIVED

JUN 11 2003

TECH CENTER 1600/2900

EV 328 518 805 US	CERTIFICATE OF MAIL BY EXPRESS MAIL	June 6, 2003
Express Mail Number		Date of Deposit
Whereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail		
Post Office to Address" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to the:		
Commissioner of Patent		
MS SEQUENCE		
Robert W. Strozier	P.O. Box, Alexandria, VA 22313-1450	June 6, 2003
		Date of Signature

**STATEMENT REGARDING SUBSTITUTE PAPER COPY OF SEQUENCE**  
**LISTING AND CRF COPY OF SEQUENCE LISTING**

Dear Sir/Madam:

In response to a 6 June 2003 Notice to Comply with Sequence Rules, Applicant used the PatentIn 3.2 software for the United States Patent and Trademark Office to generate a hard copy and an identical electronic copy of the sequences listed on Page 49, Table 1 of the application as filed. The sequence listing was also checked using Checker 3.0, with no errors reported, except that the sequences are number from 79-88 so that the sequences can append to the previously submitted sequences 1-78.

Applicant hereby asserts that the hard copy and electronic copy are identical. Please note that an electronic copy of the Checker Report is also on the diskette.

Respectfully submitted,

Date: June 6, 2003

Robert W. Strozier, Reg. No. 34,024  
Attorney for Applicants

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):



- ☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: \_\_\_\_\_

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**Applicant Must Provide:**

TECH CENTER 1600/2900

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

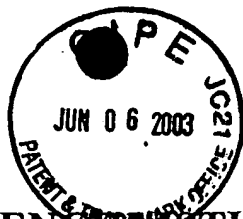
PatentIn Software Program Support

Technical Assistance.....703-287-0200

To Purchase PatentIn Software.....703-306-2600

684 1125

**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY**



## **RAW SEQUENCE LISTING** **ERROR REPORT**

BIOTECHNOLOGY  
SYSTEMS  
BRANCH



TECH CENTER 1600/2900

JAN 29 2003

RECEIVED

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/765,061C  
Source: OIP  
Date Processed by STIC: 1/7/03

RECEIVED

JUN 11 2003

TECH CENTER 1600/2900

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: [patin3help@uspto.gov](mailto:patin3help@uspto.gov) or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER**  
**VERSION 3.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND  
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202
3. Hand Carry directly to:  
U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7<sup>th</sup> Floor, Examiner Name, Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202  
Or  
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 01/29/2002

# Raw Sequence Listing Error Summary

01P8

## ERROR DETECTED

## SUGGESTED CORRECTION

SERIAL NUMBER: 09/765,061C

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1 ☒ **Wrapped Nucleics  
Wrapped Aminos** The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
- 2 ☐ **Invalid Line Length** The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3 ☐ **Misaligned Amino  
Numbering** The numbering under each 5<sup>th</sup> amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
- 4 ☐ **Non-ASCII** The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
- 5 ☐ **Variable Length** Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6 ☐ **PatentIn 2.0  
"bug"** A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s). Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
- 7 ☐ **Skipped Sequences  
(OLD RULES)** Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:  
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
This sequence is intentionally skipped  
  
Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8 ☐ **Skipped Sequences  
(NEW RULES)** Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence.  
<210> sequence id number  
<400> sequence id number  
000
- 9 ☐ **Use of n's or Xaa's  
(NEW RULES)** Use of n's and/or Xaa's have been detected in the Sequence Listing.  
Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.  
In <220> to <223> section, please explain location of n or Xaa; and which residue n or Xaa represents.
- 10 ☐ **Invalid <213>  
Response** Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
- 11 ☐ **Use of <220>** Sequence(s) missing the <220> "Feature" and associated numeric identifiers and responses.  
Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.  
(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12 ☐ **PatentIn 2.0  
"bug"** Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
- 13 ☐ **Misuse of n** n can only be used to represent a single nucleotide in a nucleic acid sequence. N is not used to represent any value not specifically a nucleotide.



Does Not Comply  
Correct No Needed

OIKE

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/765,061C

DATE: 01/07/2003

TIME: 14:04:21

Input Set : A:\SQ 09765061.txt

Output Set: N:\CRF4\01072003\I765061C.raw

3 <110> APPLICANT: The Board of Regents of the University of Texas System  
 5 <120> TITLE OF INVENTION: MUTATIONS IN A NOVEL PHOTORECEPTOR-PINEAL GENE ON 17P  
 6 CAUSE LEBER CONGENITAL AMAUROSIS (LCA4)  
 8 <130> FILE REFERENCE: 96606/16UTL  
 10 <140> CURRENT APPLICATION NUMBER: 09/765,061C  
 C--> 11 <141> CURRENT FILING DATE: 2003-01-07  
 13 <150> PRIOR APPLICATION NUMBER: 60/331362  
 14 <151> PRIOR FILING DATE: 2001-01-04  
 16 <160> NUMBER OF SEQ ID NOS: 10 — but seq. nos. were designated as 79 through 88  
 18 <170> SOFTWARE: PatentIn version 3.1

## ERRORED SEQUENCES

20 <210> SEQ ID NO: 79  
 21 <211> LENGTH: 34  
 22 <212> TYPE: DNA  
 23 <213> ORGANISM: Homo sapiens  
 25 <220> FEATURE:  
 26 <221> NAME/KEY: exon  
 27 <222> LOCATION: (1)..(34)  
 28 <223> OTHER INFORMATION: Donor Splice Site: Residue 1-10 are the exonic sequence  
 29 and Resi  
 30 dues 11-34 are the intronic sequence  
 33 <400> SEQUENCE: 79  
 E--> 34 cgg atc ccg agt gag tgg ggc cct ccg gag cag a  
 35 34  
 38 <210> SEQ ID NO: 80  
 39 <211> LENGTH: 35  
 40 <212> TYPE: DNA  
 41 <213> ORGANISM: Homo sapiens  
 43 <220> FEATURE:  
 44 <221> NAME/KEY: exon  
 45 <222> LOCATION: (1)..(35)  
 46 <223> OTHER INFORMATION: Acceptor Splice Site: Residues 1-25 are the intronic  
 47 sequence an  
 48 d Residues 26-35 are the exonic sequence.  
 51 <400> SEQUENCE: 80  
 E--> 52 cag agt gca ccg tct cgg tga cta ggt gat ctt tc  
 53 35  
 56 <210> SEQ ID NO: 81  
 57 <211> LENGTH: 35  
 58 <212> TYPE: DNA

*nucleotides must be in groups of 10<sup>lines</sup>, with enumeration on the right margin — per § 1.822(c)(2) + (6) of the M.R.*  
*— if wrapped nucleotides, see error summary sheet item 1*

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/765,061C

DATE: 01/07/2003

TIME: 14:04:21

Input Set : A:\SQ 09765061.txt

Output Set: N:\CRF4\01072003\I765061C.raw

```

59 <213> ORGANISM: Homo sapiens
61 <220> FEATURE:
62 <221> NAME/KEY: exon
63 <222> LOCATION: (1)..(35)
64 <223> OTHER INFORMATION: Donor Splice Site: Residue 1-10 are the exonic sequence
65     and Resi
66     dues 11-35 are the intronic sequence
69 <400> SEQUENCE: 81
E--> 70 csa cac cat cgt aag tag gcc ctg cgc gcc tgt ct
71     35
74 <210> SEQ ID NO: 82
75 <211> LENGTH: 35
76 <212> TYPE: DNA
77 <213> ORGANISM: Homo sapiens
79 <220> FEATURE:
80 <221> NAME/KEY: exon
81 <222> LOCATION: (1)..(35)
82 <223> OTHER INFORMATION: Acceptor Splice Site: Residues 1-25 are the intronic
83     sequence an
84     d Residues 26-35 are the exonic sequence.
87 <400> SEQUENCE: 82
E--> 88 gcc atc cat ccg ttt atc ccc aca gca cac ggg gg
89     35
92 <210> SEQ ID NO: 83
93 <211> LENGTH: 35
94 <212> TYPE: DNA
95 <213> ORGANISM: Homo sapiens
97 <220> FEATURE:
98 <221> NAME/KEY: exon
99 <222> LOCATION: (1)..(35)
100 <223> OTHER INFORMATION: Donor Splice Site: Residue 1-10 are the exonic sequence
101     and Resi
102     dues 11-35 are the intronic sequence
105 <400> SEQUENCE: 83
E--> 106 gct gct gca ggt ggg gct ggg gtt ggc agg gct gg
107     35
110 <210> SEQ ID NO: 84
111 <211> LENGTH: 35
112 <212> TYPE: DNA
113 <213> ORGANISM: Homo sapiens
115 <220> FEATURE:
116 <221> NAME/KEY: exon
117 <222> LOCATION: (1)..(35)
118 <223> OTHER INFORMATION: Acceptor Splice Site: Residues 1-25 are the intronic
119     sequence an
120     d Residues 26-35 are the exonic sequence.
123 <400> SEQUENCE: 84
E--> 124 cac tga cct gca gct ctg ggg cca ggt tga tgc cc
125     35

```

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/765,061C

DATE: 01/07/2003

TIME: 14:04:21

Input Set : A:\SQ 09765061.txt

Output Set: N:\CRF4\01072003\I765061C.raw

```

128 <210> SEQ ID NO: 85
129 <211> LENGTH: 35
130 <212> TYPE: DNA
131 <213> ORGANISM: Homo sapiens
133 <220> FEATURE:
134 <221> NAME/KEY: exon
135 <222> LOCATION: (1)..(35)
136 <223> OTHER INFORMATION: Donor Splice Site: Residue 1-10 are the exonic sequence
137     and Resi
138     dues 11-35 are the intronic sequence
141 <400> SEQUENCE: 85
E--> 142 gca gac caa ggt cag agg ccg ctg gcc acg ggg tg
143     35
146 <210> SEQ ID NO: 86
147 <211> LENGTH: 35
148 <212> TYPE: DNA
149 <213> ORGANISM: Homo sapiens
151 <220> FEATURE:
152 <221> NAME/KEY: exon
153 <222> LOCATION: (1)..(35)
154 <223> OTHER INFORMATION: Acceptor Splice Site: Residues 1-25 are the intronic
155     sequence an
156     d Residues 26-35 are the exonic sequence.
159 <400> SEQUENCE: 86
E--> 160 cat ggc tga cct tct ccc tgg gca gga gaa gcc rt
161     35
164 <210> SEQ ID NO: 87
165 <211> LENGTH: 35
166 <212> TYPE: DNA
167 <213> ORGANISM: Homo sapiens
169 <220> FEATURE:
170 <221> NAME/KEY: exon
171 <222> LOCATION: (1)..(35)
172 <223> OTHER INFORMATION: Donor Splice Site: Residue 1-10 are the exonic sequence
173     and Resi
174     dues 11-35 are the intronic sequence
177 <400> SEQUENCE: 87
E--> 178 cac cac cca ggt gcg cgg ggc tgc agg ggc gga ca
179     35
182 <210> SEQ ID NO: 88
183 <211> LENGTH: 35
184 <212> TYPE: DNA
185 <213> ORGANISM: Homo sapiens
187 <220> FEATURE:
188 <221> NAME/KEY: exon
189 <222> LOCATION: (1)..(35)
190 <223> OTHER INFORMATION: Acceptor Splice Site: Residues 1-25 are the intronic
191     sequence an
192     d Residues 26-35 are the exonic sequence.

```

RAW SEQUENCE LISTING

DATE: 01/07/2003

PATENT APPLICATION: US/09/765,061C

TIME: 14:04:21

Input Set : A:\SQ 09765061.txt

Output Set: N:\CRF4\01072003\I765061C.raw

195 <400> SEQUENCE: 88

E--> 196 gct gga tgc tcc ctg ctc ccc aca ggc atc gtg aa

197 35



## VERIFICATION SUMMARY

DATE: 01/07/2003

PATENT APPLICATION: US/09/765,061C

TIME: 14:04:22

Input Set : A:\SQ 09765061.txt

Output Set: N:\CRF4\01072003\I765061C.raw

L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:34 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:34 SEQ:79  
L:52 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:80  
L:70 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:81  
L:88 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:82  
L:106 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:83  
L:124 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:84  
L:142 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:85  
L:160 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:86  
L:178 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:87  
L:196 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:88

PAGE: 1  
06/06/2003

VERIFICATION SUMMARY REPORT

DATE:

PATENT APPLICATION

TIME:

11:33:57

INPUT SEQ: W:\Client Files\TUVW\UT HSC Houston  
\UTHou16\UTL\UTHou-16UTL 79-88.ST25.txt

GENERAL INFORMATION SECTION

-----

System 3,<110> The Board of Regents of the University of Texas

5,<120> MUTATIONS IN A NOVEL PHOTORECEPTOR-PINEAL GENE ON

17P CAUSE LEBER

6, CONGENITAL AMAUROSIS (LCA4)

8,<130> 96606/16UTL

10,<140> 09/765,061

11,<141> 2001-01-17

13,<150> 60/331362

14,<151> 2001-01-04

16,<160> 10 additional sequences, Seq. Nos. 79-88

18,<170> PatentIn version 3.2

ERRORED LINES SECTION

STATISTICS SUMMARY

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Application Serial Number: 09/765,061

Alpha or Numeric or Xml: Numeric

Application Class:

Application File Date: 2001-01-17

Art Unit:

Software Application: PatentIN3.2

Total Number of Sequences: 10

Total Nucleotides: 349

Total Amino Acids: 0

Number of Errors: 0

Number of Warnings: 0

Number of Corrections: 0

PAGE: 1  
06/06/2003

ERROR LISTING

DATE:

PATENT APPLICATION

TIME:

11:32:34

INPUT SEQ: W:\Client Files\TUVW\UT HSC Houston  
\UTHou16\UTL\UTHou-16UTL 79-88.ST25.txt